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August 17, 2004

Commissioner for Patents

Alexandria, VA 22313-1450

P.O. Box 1450

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria/JVA 22313-1450 on August 17, 2004.

Cathi H. Turner

Date of Signature:

Re: U.S. Patent Application Serial No. 10/785,374 for

THERAPEUTIC METHODS EMPLOYING NITRIC OXIDE

PRECURSORS

Our Ref. No. 1242/58

Sir:

Please find enclosed in connection with the subject U.S. patent application the following documents:

- 1. Information Disclosure Statement (2 pages);
- 2. Form PTO-1449 (7 pages) in duplicate;
- 3. Copies of cited references (49 references); and
- 4. A return-receipt postcard to be returned to us with the U.S. Patent and Trademark Office filing stamp thereon.

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

Arles A. Taylor, Jr. Registration No. 39,395

AAT/ptw/cht **Enclosures**

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Summar et al.

Group Art Unit: 1638

Serial No.: 10/785,374

Date of Signature

Examiner: Unknown

Filed: February 24, 2004

Docket No.: 1242/58

Confirmation No.: 1629

THERAPEUTIC METHODS EMPLOYING NITRIC OXIDE PRECURSORS

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INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

For:

In accordance with 37 C.F.R. 1.56, 1.97, and 1.98, applicants' undersigned attorney brings to the attention of the Patent and Trademark Office the documents listed on the attached Form PTO-1449. Copies of the references as well as Form PTO-1449 are attached hereto. This is not to be construed as a representation that a search has been made or that a reference is relevant merely because cited.

Copies of the cited documents 49-58 are of record in the file history of U.S. Patent Application Serial No. 09/585,077 filed on June 1, 2000 (now U.S. Patent No.

Serial No.: 10/785,374

6,743,823). Copies of the cited documents 59-62 are of record in the file history of U.S.

Patent Application No. 09/323,472 filed June 1, 1999 (now U.S. Patent No. 6,346,382).

The above-captioned application claims priority to U.S. Patent 6,743,823 and U.S.

Patent No. 6,346,382 under 35 U.S.C. § 120, and as per 37 C.F.R. § 1.98, no copies of

these cited documents are believed to be required.

Early passage of the subject application to issue is earnestly solicited.

Although it is believed that no fee is due, the Commissioner is hereby authorized

to charge any fees associated with the filing of this Information Disclosure Statement to

Deposit Account No. 50-0426.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

Date: 08/17/2004

By:

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AAT/ptw/cht

Enclosures

Customer No: 25297

FORM PTO-1449 U.S. Department of Commerce				At	Attorney Docket No.:		1242/58			
Patent and Trademark Office				Se	erial No.:		10/785,3	374		
List of Docu	ments C	ited by Applicant	AU6 1 9	2004	Fil	Filing Date: Februar First Named Inventor: Summa		Februar	February 24, 2004	
			S TRAI	DEMAP.	Fi			r et al.		
			·		E	kaminer:				
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			U.S.	PATENT	T DC	CUMEN	ITS		;.:	
Examiner No.		Document Nu	ımber	Date		Name		Relevant pages		
	1.	5,874,471		2/23/199	99	Waugh	, <u>, , , , , , , , , , , , , , , , , , </u>	 -		
	2.	5,891,459	-	4/6/1999	9	Cooke	et al.			
	3.	6,337,321 B1		1/8/2002	2	Cooke	et al.			
	4.	US 2002/0013288 A1 1/31/2		1/31/200	02	2 Cooke et al.				
			FOREI	GN PATE	ENT	DOCUM	IENTS			
		Document Number	Date		Coun	itry .	Name of Pai Applica		Translation Yes No	
	0	THER DOCUME	NTS (Inc	cluding Au	ıthor	r, Title, D	ate, Pertinent	Pages, E	tc.)	
	5.	Pearson et al. "Neonatal Pulmonary Hypertension," N Engl J Med, 344(24): 1832-1838 (June 12 2001).								
	6.	Gebhardt et al. "Treatment of Cirrhotic Rats with L-Ornithine-L-Aspartate Enhances Urea Synthesis and Lowers Serum Ammonia Levels," <u>The Journal of Pharmacology and Experimental Therapeutics</u> , 283(1) : 1-6 (1997).								
	7.	Kurowka, "Nitric Oxide Therapies in Vascular Diseases," <u>Current Phamaceutical Design</u> , 8 : 155-166 (2002).			naceutical					
1	8.	Morrow, "The Isoprostanes: Their Quantification as an Index of Oxidant Stress Status Vivo," <u>Drug Metabolism Reviews</u> , 32(3&4) : 377-385 (2000).				nt Stress Status in				

	U.S. Department of Commerce	Attorney Docket No.:	1242/58
Patent and Trade	emark Office	Serial No.:	10/785,374
List of Documents Cited by Applicant		Filing Date:	February 24, 2004
		First Named Inventor:	Summar et al.
		Examiner:	
	•	Group:	
9.	Suzuki et al. "Effect of Local Delivery of L-Arginine on In-stent Restenosis in Human The American Journal Of Cardiology, 89 : 363-367 (February 15, 2002).		
10.	Benedetto et al. "Increased L-citrulline/L-arginine plasma ratio in severe preclampsia," Obstet Gynecol, 96(3): 395-399 (September 2000). (ABSTRACT)		
11.	Baumgartner et al. "Hyperammonemia with reduced ornithine, arginine and praline: a new inborn error caused by a mutation in the gene encoding delta(1)-pyrroline-5-carboxylate synthase," <u>Hum Mol Genet</u> , 9(19) : 2853-2858 (November 22, 2000). (ABSTRACT)		
12.	Chwalisz et al. "Role of nitric oxide in implantation and menstruation," <u>Hum Reprod</u> , 15(suppl 3) : 96-111 (August 2000). (ABSTRACT)		
13.	Mori et al. "Reguolation of nitric oxide production by arginine metabolic enzymes," <u>Biochem Biophys Res Commun</u> , 275(3) : 715-719 (September 7 2000). (ABSTRACT)		
14.	Muriel, "Regulation of nitric oxide synthesis in the liver," <u>J Appl Toxicol</u> , 20(3) : 189-19 (May-June 2000). (ABSTRACT)		opl Toxicol, 20(3) : 189-195
15.	Bredt, "Endogenous nitric oxide synthesis: biological functions and pathophysiology," Free Radic Res, 31(6) : 577-596 (December 1999). (ABSTRACT)		
16.	Akashi et al. "Citrulline, a novel compatible solute in drought-tolerant wild watermelon leaves, is an efficient hydroxyl radical scavenger," <u>FEBS Lett</u> , 508(3) : 438-442 (November 23 2001). (ABSTRACT)		
17.	7. Ikeda et al. "Cardiovascular effects of citrullinr in ischemia/ reperfusion injury via a no nitric oxide-mediated mechanism," Methods Find Exp Clin Pharmacol, 22(7): 563-57 (September 2000). (ABSTRACT)		eperfusion injury via a non- harmacol, 22(7) : 563-571
18.	Stuhlinger et al. "Relationship boxide synthase inhibitor," JAMA	petween insulin resistance and <u>A</u> , 287(11) : 1420-1426 (March	d an endogenous nitric n 20, 2002). (ABSTRACT)

FORM PTO-1449 U.S. Department of Commerce		U.S. Department of Commerce	Attorney Docket No.:	1242/58
Patent and Trademark Office		mark Office	Serial No.:	10/785,374
List of Documents Cited by Applicant		s Cited by Applicant	Filing Date:	February 24, 2004
	·		First Named Inventor:	Summar et al.
			Examiner:	
			Group:	
19. Stuhlinger et al. " Homocysteine in asymmetric dimethylarginine," <u>Circ</u> (ABSTRACT)			e impairs the nitric oxide synt Circulation, 104(21): 2569-25	hase pathway: role of 75 (November 20, 2001)
	20.	Dulak et al. "Nitric oxide induces the synthesis of vascular endothelial growth factor by rat vascular smooth muscle cells," <u>Arterioscler Thromb Vasc</u> , 20(3) : 659-666 (March 2000). (ABSTRACT)		
	21.	Cooke, "Does ADMA cause endothelial dysfunction?" Arterioscler Thromb Vasc Biol, 20(9): 2032-2037 (September 2000). (ABSTACT)		
	22.	Cooke et al. "Atherogenesis and the arginine hypothesis," <u>Curr Atheroscler Rep</u> , 3(3) : 252-259 (May 2001). (ABSTRACT)		
	23.	Cooke, "The endothelium: a new target for therapy," <u>Vasc Med</u> , 5(1) : 49-53 (2000). (ABSTRACT)		
71.55	Boger et al. "An endogenous inhibitor of nitric oxide synthase regulates endothelia adhesiveness for monocytes," <u>J Am Cardiol</u> , 36(7) : 2287-2295 (December 2000). (ABSTRACT)			
	25.	Boger et al. "Is asymmetric dimethylarginine a novel mark of atherosclerosis?" Circulation, 101(14): 160-161 (April 11, 2000). (ABSTRACT)		
*****	26.	Uemura et al. "Rapid and efficient vascular transport of arginine polymers inhibits myointimal hyperplasia," 102(21) : 2629-2635 (November 21, 2000). (ABSTRACT)		
	27.	Jang et al. "Angiogenesis is im dimethylarginine," Circulation,	paired by hypercholesterolem 102(12): 1414-1419 (Septemb	nia: role of asymmetric oer 19 2000). (ABSTRACT
	28.	Lundman et al. "Mild-to-modera endothelial dysfunction and inc	ate hypertriglycerida in young	men is associated with

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office List of Documents Cited by Applicant		Attorney Docket No.:	1242/58	
		Serial No.:	10/785,374	
		Filing Date:	February 24, 2004	
	·	First Named Inventor:	Summar et al.	
		Examiner:		
		Group:		
29.	nia is reserved by a Cardiovasc Drugs Ther,			
30.	Chan et al. "Asymmetric dimethylarginine increases mononuclear cell adhesiveness in hypercholesterolemic humans," <u>Arterioscler Thromb Vasc Biol</u> , 20(4) : 1040-1046 (April 2000). (ABSTRACT)			
31.	Maxwell et al. "L-arginine enhances aerobic exercise capacity in association with augmented nitric oxide production," <u>J Appl Physiol</u> , 90(3) : 933-938 (March 2001). (ABSTRACT)			
32.	Maxwell et al. "Nutritional therapy for peripheral arterial disease: a double-blind, placebo-controlled, randomized trial of HeartBar," <u>Vasc Med</u> , 5(1) : 11-19 (2000). (ABSTRACT).			
33.	Schwarzacher et al. "effects of stenting on adjacent vascular distensibility and neointin formation: role of nitric oxide, " <u>Vasc Med</u> , 6(3) : 139-144 (2001). (ABSTRACT)			
34.	Schwarzacher et al "Local intramural delivery of L-arginine enhances nitric oxide generation and inhibits lesion formation after balloon angioplasty," <u>Circulation</u> , 95(7) : 1863-1869 (April 1, 1997). (ABSTRACT)			
35.	Niebauer et al. "Local L-arginine delivery after balloon angioplasty reduces monocyte binding and induces apoptosis," <u>Circulation</u> , 100(17) : 1830-1835 (October 26, 1999). (ABSTRACT)			
36.	Niebauer et al. "Gene transfer of nitric oxide synthase: effects on endothelial biology," Jam Coll Cardiol, 34(4) : 1201-1207 (October 1999). (ABSTRACT)			
37.	Kurowska, "Nitric oxide therapi (2002). (ABSTRACT)	Kurowska, "Nitric oxide therapies in vascular diseases," <u>Curr Pharm Des</u> , 8(3) : 155-166 (2002). (ABSTRACT)		
38.	Vosatka, "Persistent pulmonary hypertension of the newborn," N Engl J Med, 346(11): 864 (March 14, 2002). (ABSTRACT)			

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office List of Documents Cited by Applicant		Attorney Docket No.:	1242/58	
		Serial No.:	10/785,374 February 24, 2004	
		Filing Date:		
		First Named Inventor:	Summar et al.	
		Examiner:		
		Group:		
39.	Waugh et al. "Oral citrulline as arginine precursor may be beneficial in sickle cell disease: early phase two results," <u>J Natl Med Assoc</u> , 93(10) : 363-371 (October 2001) (ABSTRACT)			
40.	O'Connor et al. "Nonalcoholic fatty liver (NASH syndrome)," <u>Gastroenterologist</u> , 5(4) : 316-329 (December 1997). (ABSTRACT)			
41.	Bruno et al. "Population pharmacokinetics and pharmacokinetic-pharmacodynamic relationships for docetaxel," <u>Invest New Drugs</u> , 19(2) : 163-169 (May 2001). (ABSTRACT)			
42.	Gur et al. "Determination of hepatic zinc content in chronic liver sdisease due to hepatitis Bv virus," <u>Hepatogastroenterology</u> , 45(20) : 472-476 (March-April 1998). (ABSTRACT)			
43.		ure in infancy: a 14-year experi diatr, 139(6) : 871-876 (Decemb		
44.	Maier et al "Activities of urea- 57(13): 661-665 (July 3, 1979	-cycle enzymes in chronic liver 9). (ABSTRACT)	disease," <u>Klin Wochenschr</u> ,	
, 45.	Cohen et al. "The SGOT/SGI Sci, 24(11): 835-838 (Novem	PT ratioan indicator of alcohologer 1979). (ABSTRACT)	lic liver disease," <u>Dig Dis</u>	
46.	Alves et al. "The SGOT/SGP August 1981). (ABSTRACT)	T rataio in alcoholic liver diseas	se," 3(4) : 255-260 (July-	
47.	Treem et al. "Disorders of the (ABSTRACT)	e mitochondria," <u>Semin Liver Di</u>	<u>s</u> , 18(3) : 237-253 (1998).	
48.	Fearon et al. "Gonetic Analy	sis of Carbamyl Phosphate Syr	athotoco I Deficiency "	

FORM PTO 4440			<u> </u>
Patent and Trader	U.S. Department of Commerce	Attorney Docket No.:	1242/58
Tatom and Trademark Office		Serial No.:	10/785,374
List of Documents	Cited by Applicant	Filing Date:	February 24, 2004
		First Named Inventor:	Summar et al.
		Examiner:	
		Group:	
49.	Finckh et al., "Prenatal Diagnosis of Identification of a Missense Mutati 12, No. 3, pp. 206-211 (1998).	of Carbamoyl Phosphate S on in CPS1," <u>Human Muta</u>	ynthetase I Deficiency by tion, Wiley-Liss, NY, Vol.
50.	Ghishan et al., "Polymerase Chain Reaction (PCR) Detectable Polymorphisms in the Prenatal Diagnosis of Carbamyl Phosphate Synthetase I Deficiency," <u>Gastroenterology</u> , Vol. 106, No. 4 Suppl., p. A1028 (1994).		
51.	Haraguchi et al., "Cloning and Sequence of a CDNA Encoding Human Carbamyl Phosphate Synthetase I Molecular Analysis of Hyperammonemia," Gene, Vol. 107, No. 2, pp. 335-340 (1991).		
52.	Vnencak-Jones et al., "Efficacy of Prenatal DNA Testing for Carbamyl Phosphate Synthetase I Deficiency," <u>Am. Jour. Human Genetics</u> , Vol. 51, No. 4 Suppl., p. A357 (1992).		
53.	Alonso et al., "Affinity Cleavage of Carbomoyl-Phosphate Synthetase I Localizes Regions of the Enzyme Interacting with the Molecule of ATP that Phosphyorylates Carbamate," Eur. J. Biochem, p. 377-384, (1995).		
54.	Guillou et al., "Escherichia Coli Carbamoyl-Phosphate Synthetase: Domains of Glutaminase and Synthetase Subunit Interaction," Proc. Natl. Acad. Sci. USA, p. 8304-8308, (November 14, 1989).		
55.	Guy et al., "Substructure of the Amidotransferase Domain of Mammalian Carbamyl Phosphate Synthetase," J. Biol. Chem, Vol. 270 (No. 5), p. 2190-2197, (February 3, 1995).		
56.	Lagace et al., "Rat Carbamyl-Phosphate Synthetase I Gene," J. Biol. Chem, Vol. 262 (No. 22), p. 10415-10418, (August 5, 1987).		
57.	Nyunoya et al., "Characterization a Carbamyl Phosphate Synthetase I 9356, (August 5, 1985).	and Derivation of the Gene of Rat," J. Biol. Chem., Vo	Coding for Mitochondrial ol. 260 (No. 16), p. 9346-

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office List of Documents Cited by Applicant		Attorney Docket No.:	1242/58
		Serial No.:	10/785,374
		Filing Date:	February 24, 2004
		First Named Inventor:	Summar et al.
		Examiner:	
		Group:	
58.	(1997). Hoshide et al., J. Clin. Invest. Vol. 91(5), p. 1884-1887 (May 1993).		
59.			
60.			
61.	MacCallum, "Detection of PCR (1995).	R Amplified Products" PCR Es	sential Data, p. 99-127

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EXAMINER	_ DATE CONSIDERED

^{*}Examiner Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.